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PATENT AND TRADEMARK OFFICE

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**RESPONSE TO RESTRICTION  
REQUIREMENT TRANSMITTAL  
LETTER**

Docket Number  
**11245/46604**

Application Number  
**09/840,146**

Filing Date  
**April 24, 2001**

Examiner  
**Anne Halloran**

Art Unit  
**1642**

Invention Title  
**TREATMENT OF REFRACTORY HUMAN  
TUMORS WITH EPIDERMAL GROWTH  
FACTOR RECEPTOR ANTAGONISTS**

Inventor(s)  
**Harlan W. WAKSAL**

Address to:  
Commissioner for Patents  
Washington, D.C. 20231

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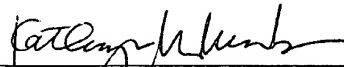
*Kathryn M. Lumb*  
Kathryn M. Lumb, Reg. No. 46,885

Transmitted herewith is a Response to the July 16, 2002 Restriction Requirement for entry in the above-identified application. This response is being timely filed.

1. No additional fees are believed to be due.
2. The Commissioner is hereby authorized to charge payment of the following fees associated with this communication or credit any overpayment to the deposit account of **Kenyon & Kenyon**, deposit account number **11-0600**:
  - A. Any additional filing fees required under 37 C.F.R. § 1.16;
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  - E. Any additional post-patent processing fees under 37 C.F.R. § 1.20; or
  - F. Any additional miscellaneous fees under 37 C.F.R. § 1.21.

3. A duplicate copy of this letter is enclosed.

Dated: August 16, 2002

By:   
Kathryn M. Lumb, Reg. No. 46,885

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PATENT  
Attorney Docket No. 11245/46604

THE UNITED STATES PATENT AND TRADEMARK OFFICE

RECEIVED

AUG 23 2002

TECH CENTER 1600/2900

Applicants: Harlan W. Waksal

Application No.: 09/840,146

Examiner: Halloran, Anne

Filing Date: April 24, 2001

Art Unit: 1642

For: Treatment of Refractory  
Human Tumors with  
Epidermal Growth Factor  
Receptor Antagonists

RESPONSE

Commissioner for Patents  
Washington, D.C. 20231

Dear Sir:

In the requirement for restriction set forth by the Office Action of July 16, 2002,

Applicant was required to elect one of the following groups of invention:

- I. Claims 36-52 in part, 53-58, 73-76 in part, and 126-127, drawn to a method of treating a tumor by administering an EGFR antagonist antibody and a chemotherapeutic agent, classified in class 424, subclass 155.1 and class 514, subclass 1.
- II. Claims 36-52 in part, 59-72, and 73-76 in part, drawn to a method of treating a tumor by administering an EGFR antagonist small molecule and a chemotherapeutic agent, classified in class 514, subclass 1.
- III. Claims 77-80 in part, and 122-125 in part, drawn to a method of treating a tumor by administering an EGFR antagonist antibody, a chemotherapeutic agent, and radiation, classified in class 424, subclass 1.11 and 155.1, and class 514, subclass 1.

CERTIFICATE OF MAILING

I hereby certify that this RESPONSE (along with any documents referred to as attached or enclosed) is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Commissioner for Patents, Washington, D.C. 20231, on the date shown below.

Date: August 16, 2002

Kathryn M. Lumb, Reg. No. 46,885

- IV Claims 77-80 in part, and 122-125 in part, drawn to a method of treating a tumor by administering an EGFR antagonist small molecule, a chemotherapeutic agent, and radiation, classified in class 424, subclass 1.11, and class 514, subclass 1.
- V. Claims 81-97 in part, 98-103, and 118-121, drawn to a method of treating a tumor by administering an EGFR antagonist antibody, and radiation, classified in class 424, subclass 1.11 and 155.1.
- VI. Claims 81-97 in part, and 104-117, drawn to a method of treating a tumor by administering an EGFR antagonist small molecule, and radiation, classified in class 424, subclass 1.11 and class 514, subclass 1.

In response, Applicant elects, with traverse, to prosecute the invention of Group I, Claims 36-52, 53-58, 73-76, and 126-127, drawn to a method of treating a tumor by administering an EGFR antagonist antibody and a chemotherapeutic agent, and reserves the right to file a divisional application directed to the non-elected subject matter. In addition, Applicant elects, with traverse, the species of a refractory tumor of the colon (colorectal cancer), as recited in claim 38. Applicant further elects, with traverse, the species of chemotherapeutic agent, irinotecan, as recited in claim 73.

Applicant respectfully submits that the restriction requirement, including species restriction, is improper for the reasons set forth herein. The Office Action sets forth a six-way restriction requirement, including species elections, of a method of treating a tumor by administering an EGFR antagonist, wherein the antagonist is either an EGFR antagonist antibody or small molecule. Applicant respectfully disagrees with Examiner for the following reasons.

An EGFR antagonist, in the context of the present invention, is any substance that inhibits stimulation of EGFR. (See Specification p. 7, ll. 3-5.) Examples of EGFR antagonists include biological molecules and small molecules (see Specification p. 7, ll. 20-28 and p. 8). Biological molecules, by definition, include, but are not limited to,

oligosaccharides and polysaccharides; oligonucleotides and polynucleotides; and oligopeptides, polypeptides, peptides, and proteins (*see* Specification p. 7, ll. 22-24). Oligopeptides, polypeptides, peptides, and proteins include, for example, antibodies, or functional equivalents of antibodies (*see* Specification p. 8, ll. 3-8). As Applicant's attorney discussed with the Examiner on August 15, 2002, an EGFR antagonist encompasses small molecules and biological molecules, which includes antibodies. Accordingly, Applicant requests that, at the least, the Examiner reconsider Groups I, III, and V to be drawn to a method of treating a tumor by administering a biological molecule EGFR antagonist and a chemotherapeutic agent and/or radiation.

There are two separate criteria that must be satisfied to support a proper restriction requirement: the invention must be independent or distinct as claimed and there must be a serious burden on the examiner if restriction is required (*See* MPEP §§ 802-03, 806, 808). The Office has not shown neither independence or distinctness of the subject matter of the pending claims nor a serious burden without restriction.

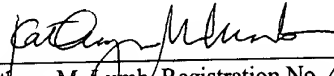
Applicant submits that the claims of Groups I-VI are sufficiently related to be properly presented in a single invention. The objective of the presently claimed invention is to provide a method of inhibiting the growth of refractory tumors that has failed or been resistant to treatment by administering to a human an EGFR antagonist in combination with a chemotherapeutic agent and/or radiation. An EGFR antagonist, in the context of the present invention, is any substance that inhibits and/or disrupts one or more of the activities normally associated with EGFR stimulation, (Specification p. 7, ll. 3-5.), which is clearly defined with a discrete mechanism of action. In addition, both chemotherapeutic agents and radiation are antineoplastic agents, which restrict the maturation and proliferation of malignant cells and thereby inhibit or prevent the growth of neoplasms or cancer. Accordingly, Applicant

submits that the subject matter of Groups I-VI is not sufficiently independent or distinct to warrant separate applications and the restriction is therefore improper. Given the commonality of the subject matter here, examination of all the claims does not place a serious search burden upon the Examiner, and applicant urges the Examiner to rejoin the claims of Group I-VI for examination as a single group.

Applicants believe that the present application is in condition for allowance, and respectfully request that the Office pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

The Office is authorized to charge any fees that may be necessary for consideration of this paper to Kenyon & Kenyon Deposit Account No. 11-0600.

Respectfully submitted,



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Dated: August 16, 2002